



Canadian Geriatrics Society

## DE-PRESCRIBING BENZODIAZEPINES IN THE ELDERLY: A REVIEW

### Abstract

Benzodiazepine medications are commonly used (often long-term) in the elderly for treatment of anxiety and insomnia despite the lack of evidence to support this practice. Not only do they lack indications but literature is reporting all benzodiazepines increase the risk of cognitive impairment, delirium, falls, fractures and motor vehicle accidents. Tapering benzodiazepines may seem like a daunting task for health care professionals but this articles will introduce a case-based approach on how to tapering and de-prescribing. Important principles include establishing indications, engaging patients, connecting with resources and providing education. While establishing an individualized tapering regime of 12.5-25 percent dose reduction every 2 weeks, emphasis on close patient monitoring with tapering protocol adjustment when necessary.

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## Historical perspective and need for de-prescribing

Benzodiazepine use began in the 1960s and peaked in the seventies.<sup>4</sup> Increasing use is being questioned, as adverse effects are becoming widely known. Benzodiazepine use is estimated at 22-27 percent in people over the age of 65 and 30 percent in those over the age of 85. More than 50 percent of benzodiazepine users do so over the long term.<sup>5</sup> Among long-term care patients, benzodiazepine use prevalence ranges from 17.7-54.1 percent in the elderly.<sup>6</sup> In those with psychiatric disorders it can range from 57-59 percent.<sup>7</sup>

The American Geriatric Society 2012 Beers Criteria update states that “older adults have increased sensitivity to benzodiazepines and slower metabolism of long-acting agents. In general, all benzodiazepines increase the risk of cognitive impairment, delirium, falls, fractures and motor vehicle accidents.”<sup>1</sup> These observations are also substantiated by the Choosing Wisely guidelines (see [Recommendation 2](#))<sup>2</sup> and the STOP/START criteria.<sup>3</sup> More information on optimal prescribing can be found in this review [here](#) and in this collection of articles [here](#).

Complications from benzodiazepine use in the elderly include a threefold increased risk of falls, dependence, adverse cognitive outcomes, an 80 percent greater risk of hip fractures vs. non-benzodiazepine users, daytime sleepiness and higher propensity to motor vehicle crashes.<sup>8</sup> In addition, elderly patients in Quebec with inappropriately prescribed benzodiazepines had a \$3,076 increase in health services compared to those correctly prescribed benzodiazepines.<sup>9</sup>

Tapering a benzodiazepine might seem like a daunting undertaking for healthcare professionals as it is for patients. In a survey of 64 health professionals, 59 (92 percent) agreed that de-prescribing guidelines for benzodiazepines would be useful.<sup>10</sup>

An article on [strategies to discontinue psychotropic medications](#) has previously been published in this journal.

In this review we build on Hogan’s article by introducing a case-based approach to de-prescribing benzodiazepines based on existing literature and additional information on aids for tapering.

### Case part 1

Mr. S. is an 83-year-old man who you have been following in your clinic for the past five years. He was widowed two years ago and lives alone in his bungalow home. His past medical history is significant for hypertension, coronary artery disease with a myocardial infarction 10 years ago treated with PCI and benign prostatic hypertrophy. He comes to see you for his routine follow-up accompanied by his son. They are both worried as his son has found him slightly more forgetful and “off-balance.” After doing a thorough history and physical examination, you review his medications and note he is using clonazepam 2 mg qhs.

### Indications for benzodiazepine prescription

Despite the prevalence of up to 25 percent use in Canadians,<sup>11</sup> benzodiazepines have the following limited indications:<sup>12-14</sup>

- Insomnia: short-term use usually two weeks
- Adjuncts to anesthesia for relaxation and amnesia
- Anxiolytic (panic disorder/agoraphobia/generalized anxiety disorder) – very short term (seven days) to short term (up to four weeks).
- Antiepileptic
- Alcohol withdrawal

Current guidelines reiterate the fact that insomnia is a short-term indication for benzodiazepines and Health Canada recommends a duration of no longer than two months including tapering period.<sup>12-15</sup> To review an article on alternative approaches in insomnia [click here](#).

## Benefits/barriers to using a tapering benzodiazepine schedule

To effectively address the benefits and barriers of tapering benzodiazepines and to determine a personalized or broad de-prescribing guideline five main questions should be asked:<sup>10</sup>

1. What is the risk of continuing the drug?
2. What is the indication or benefit of the drug?
3. What is the prevalence of overuse of the drug?
4. What are the challenges to stopping the drug?
5. What is the availability of other treatment options?

Despite the many benefits of tapering benzodiazepine use there are many practical barriers inherent in these five questions including dependence, withdrawal, patient compliance, sub-optimal non-pharmacologic and pharmacologic replacement, physician lack of knowledge or priority, lack of guidelines and fear.<sup>7</sup>

On the other hand these questions provide the basis for the benefits to tapering such as a decrease in multiple side effects including falls, poor cognition, motor vehicle crashes and pill burden with a resultant reduction of drug-drug interactions.

## Case part 2

Upon further questioning and chart review, it seems Mr. S. has been using clonazepam for the past two years. He started using it following the death of his wife due to problems with insomnia. He currently reports sleeping well; his mood is good without evidence of anxiety. He continues to be socially active and would appreciate any recommendations on how to remain well and healthy. Given his new symptoms of balance problems, subtle cognitive changes, his age and the benefits of cessation, and after discussion of the pros and cons of benzodiazepines with the patient and his son, the recommendation was made for a tapering benzodiazepine schedule.

The greatest benefit to a tapering regimen is the high success rate of cessation. Programs to taper benzodiazepines are more beneficial than cessation alone.<sup>4,8</sup> Rickles *et al.* showed that in patients who had successfully completed the discontinuation program, 73 percent were still managing without benzodiazepines three years later vs. only 39 percent in the unsuccessful taper group. Only 14 percent were able to discontinue benzodiazepines in the no-taper group.<sup>21</sup>

A **meta-analysis** by Gould *et al.* also showed significantly higher odds of not using benzodiazepines in multifaceted de-prescribing interventions and even greater success when Cognitive Behavioral Therapy (CBT) is concomitantly used.<sup>7</sup> These are only a few of many studies suggesting the benefits of tapering with added non-pharmacologic interventions.<sup>7</sup>

## De-prescribing protocols

De-prescribing protocols are varied but a few principles are ubiquitous and regarded as essential for success:

- 1. An interdisciplinary approach:** An interdisciplinary team composed of the core components of a physician, nurse and pharmacist is found to be most effective. Each patient may have different variables such as age, dependence, years of use and side effects. An interdisciplinary approach best suits such heterogeneity and includes a personalized tapering schedule.<sup>16</sup>
- 2. A multipronged approach:** Multiple reviews and meta-analyses indicate the best success in tapering benzodiazepines for insomnia is with use of CBT and a personalized benzodiazepine tapering schedule with interdisciplinary supervision. Studies that used a multifaceted approach had the greatest sustained decrease in benzodiazepine use.<sup>7-8,17-18</sup>

A part of this multifaceted approach should also include non-pharmacologic interventions, which are integral to the management of both insomnia and withdrawal of benzodiazepines.

**Table 1.** Non-Pharmacological Management of Chronic Insomnia

<b>Patient methods</b>	
1	Go to bed when tired and try to do so at the same time nightly
2	Do not use the bedroom for anything else besides sleep or intimacy
3	If there is no sleep for 20-30 minutes on initiation or after awakening then leave the bedroom
4	If not asleep for 20-30 minutes upon returning to bed, repeat step 3
5	Use alarm to wake up at the same time every morning
6	Do not nap
7	Avoid caffeine after noon
8	Avoid exercise, nicotine, alcohol and big meals within two hours of retiring to bed
<b>Healthcare provided methods/education</b>	
1	CBT (cognitive behavioural therapy) – 5-6 sessions including stimulus control, <b>sleep restriction</b> , hygiene, relaxation training and support
2	Paradoxical intention-specific cognitive therapy confronting fear of staying awake and its effects to eliminate anxiety about sleep performance
3	Biofeedback-control physiologic variable through visual/auditory feedback to reduce somatic arousal

Adapted from Clinical guideline for the evaluation and management of chronic insomnia in adults. Schute-Rodin, S. *et al. J. Clin. Sleep Med.* 2008 Oct 15; 4(5) and [here](#).

**Table 2.** Principles of Primary-care Management in Tapering Benzodiazepines

<b>Establish Indication</b>	Review prescription record. Establish an indication for long-term benzodiazepine use. If no indication, discuss tapering.
<b>Engage Patients</b>	Provide letter/brochure suggesting methods of tapering. Set up follow-up schedule with health professionals. Empower patients to take control over their treatment.
<b>Connect to Resources</b>	Refer patients to additional agencies/support groups: health services, local community and mental health services. Alcohol services are appropriate if concomitant alcohol misuse with benzodiazepine dependence. Cigarettes are even more difficult to give up permanently than benzodiazepines. Postpone smoking cessation until after benzodiazepines are tapered.
<b>Provide Education</b>	Suggest changes in lifestyle such as regular exercise and keeping a regular routine throughout the week, including weekends.

Adapted from Withdrawing Benzodiazepines in Primary Care. Lader, M. *et al. CNS Drugs.* 2009; 23(1), **Strategies for discontinuing long-term benzodiazepine use.** Voshaar, R.C. *et al. The British Journal of Psychiatry.* 2006; 189 (3) and Pottie K., Thompson W., *et al.*

**3. An ability to customize and attain flexibility in a tapering regimen:** A taper off benzodiazepines can require anywhere from four weeks to one year depending on such factors as patient age, co-morbidities, dependence, supports and episodes of withdrawal.<sup>4</sup> It is wise to taper off as fast as safely possible to avoid the myriad of complications with this class of medication. An example of a brisk schedule might be 8-12 weeks at a rate of 12.5-25 percent per week.<sup>8</sup> Tapering off too slowly may have the effect of making the withdrawal the focus of patients’ existence. If patients fail after investing so much into the process, they may be less inclined to proceed in the future. Physicians need to be sensitive and inclusive of patients’ own values and concerns.

The bulk of the literature suggests a 25 percent reduction in two-week increments over eight weeks.<sup>4,7-8,12,19</sup> A dose decrement of 12.5 percent every two weeks can also be used when withdrawal symptoms are experienced. Ideally the lower/slower dose reduction of 12.5 percent should take place near the end of the taper, as withdrawal is harder to tolerate at the last stages of the tapering regimen.<sup>8,19</sup> Patients should be seen weekly or every two weeks and assessed by a physician. If there are signs of withdrawal a more flexible tapering schedule can be instituted.<sup>4,7,19</sup>

- 4. An emphasis on patient-led (empowered) self-care:** The most useful component to tapering benzodiazepines is a patient-empowered, self-led approach toward taking steps to accomplish this goal. Even simple interventions are helpful. In the **EMPOWER trial**, patients were randomized to receive a simple booklet that gave suggestions to help taper benzodiazepines, suggested alternate aids for insomnia and anxiety and examples of a tapering schedule. At six months, 27 percent of the intervention group had discontinued benzodiazepine use compared with 5 percent of the control group. This was done with the additional benefit of involving healthcare professionals, in this case pharmacists, in the education and delivery of this information.<sup>23</sup>

**Table 3.** Comparison of Benzodiazepines

Agent	Oral total daily dose (mg)	Comparative potency (mg)	Range of potency	Time to peak level (hours)	Half-life (hours)
Alprazolam	0.5-6	0.5		1-2	12
Bromazepam	6-30	3	(3-7.5)	1-4	20
Chlordiazepoxide	5-100	25	(10-25)	1-4	100
Clonazepam	0.5-4	0.25	(0.25-0.5)	1-4	34
Clorazepate	16-60	10	(7.5-10)	0.5-2	100
Diazepam	4-40	5		1-2	100
Flurazepam*	15-30	15	(5-15)	0.5-1	100
Lorazepam	0.5-6	1		1-4	15
Nitrazepam*	5-10	2.5	(2.5-5)	0.5-2	30
Oxazepam*	30-120	15	(15-30)	1-4	8
Temazepam*	7.5-30	10	(5-10)	2-3	11
Triazolam*	0.125-0.25	0.25	(0.1-0.25)	1-2	2

\*Agents used commonly in insomnia.

Adapted from Benzodiazepines, Oral: Comparison Chart-Drug Information (Ottawa Hospital Formulary)

### Case part 3

Keeping these principles in mind, Mr. S. and his primary physician, in consultation with his pharmacist, embarked on a tapering schedule with a flexible goal to stop his clonazepam use in 16 weeks. They chose a longer schedule due to the potency of clonazepam and patient preference. He has drug-free days built into his regimen as well as clonazepam as needed for withdrawal symptoms.

**Mr. S. Clonazepam tapering schedule**

<b>Week</b>	<b>Dosage (mg hs)</b>	<b>Breakthrough</b>	<b>drug-free days</b>
0-Baseline	2	clonazepam 0.125 mg by mouth as needed for taper flexibility if withdrawal symptoms present (start week 2)	Start drug-free nights as tolerated (week 8)
1-Taper start	1.75		
2	1.5		
4	1.25		
6	1		
8	0.75		
10	0.5		
12	0.375		
14	0.25		
16	0.125		
18	STOP		

In addition he starts CBT for both insomnia and cessation of benzodiazepines. Follow-up with his primary care physician occurs every two weeks (either on the phone or in person). Follow-up can also be facilitated by other allied care team members such as a nurse, social worker, pharmacist and psychologist depending on specific needs and the resources available.

**Case part 4**

Mr. S. feels ready to start his taper but wants to know if he should monitor anything specific during his taper.

**Monitoring during taper**

Benzodiazepine withdrawal symptoms are common especially the longer they are used. For long-term use of six months or beyond, approximately 40 percent of users experience moderate to severe withdrawal symptoms. The remaining 60 percent experience mild symptoms,<sup>27</sup> which can be very broad and may include tremors, anxiety, perceptual disturbances, dysphoria, psychosis and seizures.<sup>30</sup>

In the case of Mr. S., his withdrawal symptoms may logically manifest as insomnia. The **Insomnia Severity Index** is a useful tool, especially in conjunction with a parallel Insomnia Severity Index Scale for a patient's partner. These scales can be used when clinically apparent quantitative or qualitative sleep disturbance is noted. Another valuable and simple tool to monitor sleep quality and effectiveness of the benzodiazepine taper is a sleep diary filled daily by the patient and reviewed at each visit.<sup>18,20</sup> An example of a sleep diary can be accessed [here](#). More information on insomnia can be found [here](#).

Co-morbid medical and psychiatric conditions such as obstructive sleep apnea, congestive heart failure and depression may cause pseudo-withdrawal symptoms such as dyspnoea, pain, nocturia or anxiety. Untreated, these conditions frequently contribute to insomnia and may also masquerade as benzodiazepine withdrawal. This illustrates the fact that symptoms of withdrawal are not always as they seem and other causes must be explored and mitigated.

A few clinical scales can be used to assess for benzodiazepine withdrawal symptoms themselves. There is no cluster of symptoms that completely predicts withdrawal. A review of data from patients withdrawing from benzodiazepines has identified a few key symptoms that help confirm the presence of withdrawal and show when the symptoms may typically occur.<sup>23,26</sup> Some of the most common symptoms include depression, tremor, noise sensitivity, muscle pains, malaise and dizziness.

The **CIWA-B scale** is helpful because it combines objective healthcare providers' and subjective patients' view of the symptoms of withdrawal. The benzodiazepine withdrawal symptoms questionnaire or **BWSQ 2** is another helpful tool. It is a subjective scale validated in other studies as an effective tool for measuring withdrawal symptoms.<sup>23,26,28</sup>

It comprises 20 questions graded by severity (no symptoms-0, moderate-1 and severe-2) and has a maximum score of 40. A score of 3 or greater is usually associated with true withdrawal symptoms.<sup>26</sup>

### Case part 5

Mr. S. starts successfully into his regimen but by week six he starts to have insomnia and withdrawal symptoms including irritability, anxiety and headache. He is asking you what should be done.

After correctly identifying withdrawal symptoms vs. pseudo-withdrawal symptoms (those associated with another underlying cause), the taper rate can be reduced and/or additional as needed (PRN) benzodiazepine such as clonazepam 0.125 mg po hs can be added.

In studies validating the BWSQ 2, the questionnaire was applied to a tapering regimen of 25 percent over two-week periods.<sup>26,28</sup> This is helpful in the case of Mr. S. as he is on this regimen and the results can be applied most closely to his situation. Most studies also support this taper approach.<sup>4,7-8,12,19</sup> Keep in mind that other methods such as CBT can also be introduced or intensified as detailed above to aid in the tapering process.

### Case part 6 (summary)

Mr. S. starts using as needed clonazepam, more intensive CBT and sleep hygiene with success. He is able to taper off his clonazepam by 26 weeks after slowing his taper to a 12.5 percent reduction over two weeks.

### Conclusion

Benzodiazepines have various deleterious effects in the elderly and often few indications for ongoing use. A tapering schedule of 25 percent dose reductions over two-week periods for approximately 12 weeks is a good rule of thumb but the process is highly variable depending on the dosage, co-morbid disease, length of use and patient preference. If there are difficulties in tapering, the addition of small, as needed, doses of benzodiazepine and a reduction in tapering rate should be used particularly near the end of the taper when withdrawal symptoms are most likely to occur. The best results are achieved with concomitant CBT and a team-based approach. Successful de-prescribing in this manner can be achieved in approximately 77 percent of patients.<sup>18,22</sup> The principles of de-prescribing benzodiazepines apply to other medications of long-term use such as opioids and it is imperative we include these practices in the clinical setting to educate our patients and keep them safe. In the year 2000 cost estimates for fall-related injuries in the elderly from benzodiazepine were nearly 3 billion dollars in the U.K.<sup>29</sup> Consequently, de-prescribing may reduce the high financial costs these drug harms have on our healthcare system.<sup>31</sup>

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